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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/629,266	07/29/2003	Yeyan Zhang	U0158P OS/OAPT (1010-93)	8587
23657	7590	07/13/2006	EXAMINER	
COGNIS CORPORATION PATENT DEPARTMENT 300 BROOKSIDE AVENUE AMBLER, PA 19002			PROUTY, REBECCA E	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 07/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/629,266

Applicant(s)

ZHANG ET AL.

Examiner

Rebecca E. Prouty

Art Unit

1652

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 May 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) 2,3,7-16,20 and 26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4-6,17-19,21-25 and 27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>8/04,9/04</u> . | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1652

Applicant's election with traverse of Group I, Claims 1, 4-6, 17-19, 21-25 and 27 in the reply filed on 5/1/06 is acknowledged. The traversal is on the ground(s) that Groups I and II should be rejoined into one group since the subject matter of both groups is the same, namely a method of converting a fatty acid to its corresponding dicarboxylic acid using a yeast transformed with fusion gene comprising a POX 4 promoter. This is not found persuasive because Groups I and II are not drawn to the same subject matter. Group II is drawn to a method of transforming a yeast cell while Group I is drawn to methods of converting a fatty acid to its corresponding dicarboxylic acid. As previously indicated methods of transforming a yeast cell and methods of converting a fatty acid to its corresponding dicarboxylic acid are separately classifiable. Separate classification is *prima facie* evidence of serious burden of search (see MPEP 803).

The requirement is still deemed proper and is therefore made FINAL.

Claims 2, 3, 7-16, 20, and 26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 5/1/06.

Art Unit: 1652

Claims 1, 4-6, 17-19, 21-25 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to methods of converting a fatty acid to its corresponding dicarboxylic acid using a genus of POX4 promoters or promoters of a yeast gene induced when the yeast is grown on fatty acids or alkanes. The specification teaches the structure of only a single representative species of such promoters, i.e., the *C. tropicalis* POX4 promoter. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of promoting expression of a yeast gene induced when the yeast is grown on fatty acids or alkanes. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Art Unit: 1652

Claims 1, 4-6, 17-19, 21-25 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to methods of converting a fatty acid to its corresponding dicarboxylic acid using a genus of target genes involved in dicarboxylic acid production. The specification teaches the structure of only a three representative species of such genes, i.e., the *C. tropicalis* CYP52A2A gene, the *C. tropicalis* CYP52A5A gene, and the *C. tropicalis* NCP1B gene. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of involvement in dicarboxylic acid production. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Art Unit: 1652

Claims 1, 4-6, 17-19, 21-25 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of converting a fatty acid to its corresponding dicarboxylic acid using a *C. tropicalis* POX4 promoter fused to at least one of the *C. tropicalis* CYP52A2A gene, the *C. tropicalis* CYP52A5A gene, and the *C. tropicalis* NCP1B gene, does not reasonably provide enablement for methods of converting a fatty acid to its corresponding dicarboxylic acid using any POX4 promoter or any promoter of a yeast gene induced when the yeast is grown on fatty acids or alkanes fused to any gene involved in dicarboxylic acid production. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 1 and 17-18 are so broad as to encompass methods of converting a fatty acid to its corresponding dicarboxylic acid using any POX4 promoter or any promoter of a yeast gene induced when the yeast is grown on fatty acids or alkanes fused to any gene involved in dicarboxylic acid production. Claims 4-6 and 21-25 further limit the scope of the gene involved in dicarboxylic acid production to any member of an ω -hydroxylase complex (Claim 4), any CYP, NCP or CTTb5 gene (Claims 5, 21, 23-25 and 27) or any CYP52A2A, CYP52A5A, NCP1B, or CYTb5 gene

Art Unit: 1652

(Claims 6 and 22) while claims 19 and 25 further limit the scope of the promoter to any promoter of a *C. tropicalis* gene induced when the yeast is grown on fatty acids or alkanes. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of promoters and genes involved in dicarboxylic acid production broadly encompassed by the methods of the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence or a promoter's nucleotide sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification) or which nucleotides in a promoter's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification) and detailed knowledge of the ways in which the proteins' or promoters' structure relates to its function. However, in this case the disclosure is limited to the using a *C. tropicalis* POX4 promoter fused to at least one of the *C. tropicalis* CYP52A2A gene, the *C. tropicalis* CYP52A5A gene, and the *C. tropicalis* NCP1B gene.

Art Unit: 1652

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made or in a promoter's sequence where nucleotide modification can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein/promoter and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass methods of converting a fatty acid to its corresponding dicarboxylic acid using any POX4 promoter or any promoter of a yeast gene induced when the yeast is grown on fatty acids or alkanes fused to any gene involved in dicarboxylic acid production because the specification does not establish: (A) regions of the protein structure of any gene involved in dicarboxylic acid production which may be modified without effecting its activity; (B) the general tolerance of gene involved in dicarboxylic acid production to modification and extent of such tolerance; (C) a rational and predictable

Art Unit: 1652

scheme for modifying any amino acid residues of any gene involved in dicarboxylic acid production with an expectation of obtaining the desired biological function; and (D) regions of the *C. tropicalis* POX4 promoter which may be modified without effecting its activity; (E) the general tolerance of the *C. tropicalis* POX4 promoter to modification and extent of such tolerance; (F) a rational and predictable scheme for modifying the *C. tropicalis* POX4 promoter with an expectation of obtaining the desired biological function; and (G) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including methods of converting a fatty acid to its corresponding dicarboxylic acid using any POX4 promoter or any promoter of a yeast gene induced when the yeast is grown on fatty acids or alkanes fused to any gene involved in dicarboxylic acid production. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of promoters and genes having the desired biological characteristics is unpredictable and the

Art Unit: 1652

experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 4-6, 17-18, 21-24, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Wilson et al. (WO 00/20566).

Wilson et al. teach methods of converting a fatty acid to its corresponding dicarboxylic acid comprising transforming a suitable host cell with a gene encoding CYP52A2A or CYP52A5A and culturing the cell in the presence of an organic substrate that is biooxidizable to a mono- or polycarboxylic acid, such as saturated or unsaturated fatty acids, alkanes, alkenes, alkynes

Art Unit: 1652

or combinations thereof (see pages 13-15 and 24). Wilson teach that the existing promoter of the CYP genes can be replaced with a strong promoter and teach that a suitable example of such a strong promoter is the *Candida* POX4 promoter (see page 22) and that suitable host cells include yeast.

Claims 1, 4-6, 17-18, 21-24, and 27 are rejected under 35 U.S.C. 102(a or e) as being anticipated by Wilson (US Patent 6,331,420).

Wilson et al. teach methods of converting a fatty acid to its corresponding dicarboxylic acid comprising transforming a suitable host cell with a gene encoding CYP52A2A or CYP52A5A and culturing the cell in the presence of an organic substrate that is biooxidizable to a mono- or polycarboxylic acid, such as saturated or unsaturated fatty acids, alkanes, alkenes, alkynes or combinations thereof (see columns 9-11 and column 17).

Wilson teach that the existing promoter of the CYP genes can be replaced with a strong promoter and teach that a suitable example of such a strong promoter is the *Candida* POX4 promoter (see column 16) and that suitable host cells include yeast.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

Art Unit: 1652

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 19 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of Wilson et al. (US Patent 6,331,420) or Wilson et al. (WO 00/20566) in view of Okazaki et al.

Wilson et al. (US Patent 6,331,420) and Wilson et al. (WO 00/20566) are discussed above. They do not teach the *Candida tropicalis* POX4 promoter.

Okazaki et al. teach the *Candida tropicalis* POX4 promoter

Art Unit: 1652

and teach that the POX4 gene is induced by growth on fatty acids or alkanes.

Therefore, it would have been obvious to one of ordinary skill in the art to use the *Candida tropicalis* POX4 promoter of Okazaki et al. in the methods of Wilson et al. (US Patent 6,331,420) or Wilson et al. (WO 00/20566) as each of the Wilson et al. references specifically suggest use of a POX4 promoter for the overexpression of the *CYP52A2A* or *CYP52A5A* genes.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca E. Prouty whose telephone number is 571-272-0937. The examiner can normally be reached on Tuesday-Friday from 8 AM to 5 PM. The examiner can also be reached on alternate Mondays

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Rebecca Prouty
Primary Examiner
Art Unit 1652